IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF UTAH

NORTHERN DIVISION

ELAINE J. SHIPLEY, Plaintiff, vs. FOREST LABORATORIES, INC., Defendant.	ORDER AND MEMORANDUM DECISION Case No. 1:06-cv-00048-TC

Plaintiff Elaine Shipley's husband, Kurt Shipley, took his own life on April 29, 2004, seventeen days after he began taking the antidepressant drug, Lexapro. Approximately two years after Mr. Shipley's death, Mrs. Shipley filed this wrongful death action against Defendant Forest Laboratories, Inc. (Forest), alleging that Forest failed to warn Mr. Shipley and his health care providers about the risks associated with Lexapro, particularly "the potential for [Lexapro] to induce its users to commit, or attempt to commit, suicide." (Compl. at 2-3, Dkt. No. 1.)

On June 14, 2006, this case was transferred to the Multi-District Litigation Panel in the Eastern District of Missouri, MDL No. 1736, In re: Celexa and Lexapro Products Liability Litigation. The case was remanded and reassigned to this court on August 27, 2013.

Forest has filed a motion to exclude the expert testimony of Dr. George Glass (Dkt. No. 78), along with two motions for summary judgment (Dkt. Nos. 79 and 80). On March 4, 2015, the court heard testimony from Dr. Glass to determine whether he qualifies as an expert under Rule 702 of the Federal Rules of Evidence and under Daubert v. Merrill Dow Pharmaceuticals,

Inc., 509 U.S. 579 (1993). The court also heard oral argument on Forest's motions for summary judgment. For the reasons explained below, the court DENIES Forest's Motion to Exclude the Testimony of George S. Glass, M.D. (Dkt. No. 78); DENIES Forest's Motion for Summary Judgment Based on Federal Preemption (Dkt. No. 79); and GRANTS IN PART AND DENIES IN PART Forest's Motion for Summary Judgment (Dkt. No. 80).

FACTUAL BACKGROUND[1]

I. Lexapro Labeling History

In August 2002, the United States Food and Drug Administration (FDA) approved the new drug application for Lexapro. Lexapro is manufactured by Forest Laboratories Ireland Limited. (Weinberger Decl. ¶ 4, Dkt. No. 80-66.) Forest Laboratories, Inc. (the Defendant in this case), is the U.S. sponsor for Lexapro. (Id. ¶ 5.) In addition, "[w]arnings for Lexapro are drafted by the regulatory affairs department of Forest Laboratories, Inc." (Id. ¶ 6.)

Lexapro is in a class of prescription antidepressant drugs known as "selective seratonin reuptake inhibitors" (SSRIs). The FDA and the scientific and medical communities commonly treat SSRIs as a class. In 2003, GlaxoSmithKline requested FDA approval for pediatric use of its SSRI, Paxil. In its review of the clinical trial data for the Paxil pediatric supplement, the FDA found that a number of adverse events involved suicidal behavior or ideation but had not been designated as such. The FDA requested clarification of the data, and GlaxoSmithKline's

[1] The facts are taken from the parties' briefing on Forest's motions for summary judgment, with the court identifying disputes of material fact where they may exist. Because she is the nonmoving party, the court recounts the facts and all reasonable inferences from those facts in the light most favorable to Mrs. Shipley. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587 (1986); Applied Genetics Int'l, Inc. v. First Affiliated Sec., Inc., 912 F.2d 1238, 1241 (10th Cir. 1990).

reanalysis indicated an increase in suicidal thoughts and behaviors with the use of Paxil in pediatric clinical trials. To determine whether the increase in suicidality applied to other SSRIs, the FDA asked other drug sponsors, including Forest, to reanalyze their own pediatric data.

In February 2004, after receiving the results of the requested reanalysis, the FDA convened an advisory committee to discuss "the relationship, if any, between treatment of pediatric patients with antidepressant drugs and suicidal behavior." (Comm. Meeting Tr. 19, Feb. 2, 2004, Dkt. No. 94-3.) The FDA explained, "we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully." (Id. 24.)

Based on the committee's recommendations, the FDA issued a Public Health Advisory on March 22, 2004, indicating that it had asked sponsors of certain antidepressant drugs (including Lexapro) to update labels to include "a statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality." (FDA Public Health Advisory, Mar. 22, 2004, Dkt. No. 78-31.) The updated warning would advise health care providers to "carefully monitor patients receiving antidepressants for possible worsening of depression or suicidality, especially at the beginning of treatment" and to "instruct patients, their families and their caregivers to be alert" for emerging suicidality and to immediately report such symptoms. (Id.)

Three days before issuing the Public Health Advisory, the FDA wrote to Forest asking for updates to the Lexapro label to "caution practitioners and patients about the need for close observation of patients being treated with antidepressants," particularly for worsening depression, suicidality, and other symptoms that may precede suicidality. (Letter from FDA to Forest, Mar. 19, 2004, Dkt. No. 80-92.) The FDA requested the following relevant revisions:

> Under **WARNINGS**, we are requesting the addition of a new subsection entitled **Clinical Worsening and Suicide**. Please note that the title of this new section should be bolded, as well as two statements embedded in this labeling language.
>
> **Warnings - Clinical Worsening and Suicide**
>
> Patients with major depressive disorder, both adult and pediatric, can experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.
>
> Although there has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. **Nevertheless, patients being treated with antidepressants should be observed closely for worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases.** Consideration should be given to discontinuing the medication in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.
>
> . . .
>
> **Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications should be alerted about the need to monitor patients for the emergence of agitation, irritability, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers.** . . .

(Id.)

Responding to the letter, Forest suggested edits to the warning, and on April 19, 2004, the FDA responded with its own revisions, which became the final warning label. The edits added some language but did not substantively change the bolded sections. The FDA stated that the new labeling "should be implemented immediately, and submitted as a CBE supplement."[2] (See Email from Paul David to Andrew Friedman (Apr. 19, 2004), Dkt. No. 80-93.) On April 30,

[2] "CBE" stands for "changes being effected" and refers to a regulation that allows drug manufacturers to update labels under certain circumstances before obtaining FDA approval.

2004, Forest sent its final label to the FDA and indicated its intent to include the new label in Lexapro packages on May 31, 2004. The FDA approved the changes on May 20, 2004.

II. Kurt Shipley's Lexapro Use

Kurt Shipley first took Lexapro in June 2003, when Dr. Michael Kirkham gave Mr. Shipley some samples based on a diagnosis of "anxiety syndrome, panic disorder and depression, with physical symptoms of palpitations." (Kirkham Dep. at 49, Dkt. No. 78-42.) Lexapro appeared to help Mr. Shipley, and, according to Mr. Shipley's medical records, he took Lexapro from about June to October 2003. (Shipley Dep. at 116-17, Dkt. No. 78-44.)

Mr. Shipley did not begin taking Lexapro again until April 2004. At this time, the Lexapro label did not include the updated, bolded warning language related to suicide. The April 2004 label merely warned that "[t]he possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high risk patients should accompany initial drug therapy." (Lexapro Label at 7, Dkt. No. 80-73.)

On April 12, 2004, Mr. Shipley saw Nurse Practitioner Carl Christensen and reported having business problems and symptoms of anxiety, such as palpitations, insomnia, shortness of breath, sweating, and irritability. Nurse Christensen diagnosed "general anxiety disorder or mixed anxiety with depression" and prescribed Lexapro. (Christensen Dep. at 54, Dkt. No. 78-45.) At a follow-up visit with Nurse Christensen on April 14, 2004, Mr. Shipley reported that he was doing better and did not report any concerns about Lexapro.

On April 27, 2004, Mr. Shipley told his wife that he felt his condition was getting worse. So Mrs. Shipley made an appointment for Mr. Shipley to see Dr. Craig Julien that day. At his visit with Dr. Julien, Mr. Shipley reported concerns about fatigue, inability to get work done, and

financial stress. Mr. Shipley also explained that he was having "horrendous thoughts," which "triggered the concern of suicidality" for Dr. Julien. (Julien Dep. at 47, Dkt. No. 78-48.) When Dr. Julien explicitly asked about suicide, Mr. Shipley "said that he had a good stout spirit and that he would never do that." (Id.) Dr. Julien did not pursue the issue further. Dr. Julien continued Mr. Shipley's prescription for Lexapro and added a prescription for Wellbutrin.

On April 29, 2004, Mr. Shipley committed suicide. Mrs. Shipley, personally and on behalf of Mr. Shipley's estate, now seeks to recover damages resulting from Mr. Shipley's death.

ANALYSIS

Forest filed three motions that the court will address in turn: a Motion to Exclude the Testimony of George S. Glass, M.D. (Dkt. No. 78); a Motion for Summary Judgment Based on Federal Preemption (Dkt. No. 79); and a Motion for Summary Judgment (Dkt. No. 80).

I. Motion to Exclude Dr. Glass

To succeed on her failure to warn claim,[3] Mrs. Shipley must prove causation. House v. Armour of Am., Inc., 929 P.2d 340, 346 (Utah 1996). In prescription drug cases, the causation element requires proof, usually in the form of expert testimony, of both general and specific causation. See Coburn v. Smithkline Beecham Corp., 174 F. Supp. 2d 1235, 1239 (D. Utah 2001) (recognizing the need for expert testimony on general and specific causation). "General causation is whether a substance is capable of causing a particular injury or condition in the general population and specific causation is whether a substance caused a particular individual's injury." Norris v. Baxter Healthcare Corp., 397 F.3d 878, 881 (10th Cir. 2005).

[3] Mrs. Shipley concedes that summary judgment should be granted on her design defect and manufacturing defect claims, which leaves failure to warn as the sole claim for the court to address.

Mrs. Shipley has retained Dr. David Healy to address general causation. Dr. Healy will testify that Lexapro "can make individuals who may not have been likely to commit suicide before taking the pill, more likely to do so while on a course of treatment." (Healy Report at 1, Dkt. No. 90-4.) Mrs. Shipley also plans to call Dr. George Glass, who will testify that Mr. Shipley's condition worsened during the time he took Lexapro and use of the drug was "a significant contributing factor to his death by suicide." (Glass Report at 9, Dkt. No. 78-57.) Forest previously moved to exclude Dr. Healy's general causation testimony, but the MDL court denied the motion. In re Celexa & Lexapro Prods. Liab. Litig., 927 F. Supp. 2d 758, 768 (E.D. Mo. 2013). Forest now seeks to exclude Dr. Glass's expert testimony on specific causation.

A. Legal Standards

Expert opinions are admissible if "(1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case." Fed. R. Evid. 702. The standard under Rule 702 is "liberal," United States v. Gomez, 67 F.3d 1515, 1526 (10th Cir. 1995), but "[t]he proponent of expert testimony bears the burden of showing that the testimony is admissible." Conroy v. Vilsack, 707 F.3d 1163, 1168 (10th Cir. 2013). To determine whether the proponent has met its burden, the court applies a two-part test. First, the court decides whether the witness is "qualified by knowledge, skill, experience, training, or education to render an opinion." Id. (quotations omitted). "Second, if the expert is sufficiently qualified, the court must determine whether the expert's opinion is reliable under the principles set forth in *Daubert*." 103 Investors I, L.P. v. Square D Co., 470 F.3d 985, 990 (10th Cir. 2006).

B. Qualifications

Forest does not challenge Dr. Glass's qualifications to testify about specific causation. Dr. Glass is a board-certified psychiatrist who has practiced for more than forty years. In his clinical experience, Dr. Glass has treated patients with SSRIs and has seen suicidality related to use of SSRIs. In addition, Dr. Glass has published at least one article about the side effects of SSRIs. With this background, Dr. Glass is well qualified to testify as a specific causation expert.

While Forest concedes Dr. Glass's credentials in the area of specific causation, Forest maintains that Dr. Glass is not qualified to testify as a labeling expert. At oral argument, Mrs. Shipley's counsel confirmed that Dr. Glass will not be offered as an expert in FDA labeling or other regulatory requirements. But Dr. Glass may be asked to explain how a practicing physician would react to the various Lexapro labels. The court concludes that Dr. Glass may only testify about how he considers and responds to warning labels and label changes in his own practice. Dr. Glass may not speculate or testify about how Dr. Julien, Nurse Christensen, or any other provider would have reacted to a change in the Lexapro label.

C. Reliability

Even if a witness is qualified to testify about a particular topic, the witness's opinions must still be reliable, or "based upon sufficient facts or data" and "the product of reliable principles and methods." Fed. R. Evid. 702. In other words, the court must determine whether an expert's testimony will be helpful to the trier of fact, which "entails a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and whether that reasoning or methodology properly can be applied to the facts in issue." Daubert, 509 U.S. at 592-93. Forest challenges the reliability of Dr. Glass's methodology and opinions,

first by arguing that Dr. Glass's opinions are not consistent with Dr. Healy's general causation opinions.[4] Second, Forest maintains that Dr. Glass failed to perform the necessary differential diagnosis. Finally, Forest contends that Dr. Glass's opinions are unreliable because he cannot rule out Wellbutrin, another drug that Mr. Shipley was taking, as the cause of his suicide.

I. General and Specific Causation

Based on his review of the medical records and other evidence, Dr. Glass opined that the primary method by which Lexapro contributed to Mr. Shipley's death was through worsening depression. Mrs. Shipley's general causation expert, Dr. Healy, identified three mechanisms by which Lexapro induces suicidality: akathisia, psychotic decompensation, and emotional deregulation (also known as "emotional blunting"). Forest argues that worsening depression does not fit within any of these three categories, and as a result, there is no admissible general causation evidence supporting Dr. Glass's worsening depression theory.

The court disagrees. Although Dr. Healy listed akathisia, emotional blunting, and psychotic decompensation as three "mechanisms of suicide induction," (Healy Report at 35), he also explicitly stated that "[t]he symptoms experienced by those adversely affected prior to suicide include worsening depression . . . ." (Id. at 1.) Dr. Glass's opinion that Mr. Shipley experienced worsening depression is entirely consistent with Dr. Healy's opinion that worsening depression is a common symptom before a Lexapro-induced suicide.

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[4] Forest has made the same argument in at least two other cases. And in both cases, the courts rejected Forest's position and held that Dr. Glass's opinions were consistent with Dr. Healy's general causation opinions. See Bennett v. Forest Labs., Case No. 2:06-cv-72-FtM-38DNF (M.D. Fla. Apr. 9, 2015), Dkt. No. 120-1; Cross v. Forest Labs., Case No. 1:05-cv00170-MPM-SAA (N.D. Miss. Feb. 19, 2015), Dkt. No. 104-1. As explained below, the court agrees with these decisions.

Moreover, Dr. Glass explained that, in addition to worsening depression, Mr. Shipley exhibited aspects of akathisia and emotional blunting. Before his visits with Nurse Christensen, Mr. Shipley experienced insomnia and pacing, both of which are signs of akathisia. These symptoms "got worse and worse and worse" after Mr. Shipley began taking Lexapro. (Shipley Dep. at 160-61, Dkt. No. 90-6.) Indeed, while on Lexapro, Mr. Shipley excessively paced back and forth, including during the middle of the night. (Id. at 161.) In addition, Mr. Shipley was originally diagnosed with anxiety, but his anxiety reduced with his use of Lexapro. As Dr. Glass testified, anxiety reduction is a sign of emotional blunting, as is the act of suicide itself, both of which occurred with Mr. Shipley. (Hr'g Tr. 54-55, 57.) Dr. Glass also clarified that many of the signs of worsening depression are also symptoms of emotional blunting; these include inability to make decisions, lack of energy, pacing, and insomnia. (Id. 61.)

Although Dr. Healy gave akathisia, emotional blunting, and psychotic decompensation as three specific ways by which Lexapro may induce suicidality, these are only "the most commonly cited but not the exclusive candidates for leading to problems and in fact these mechanisms are likely to operate in combination rather than entirely independently." (Healy Report at 35.) Dr. Glass reiterated this same idea and explained that, in Mr. Shipley's case, the three mechanisms combined together and with other symptoms—primarily worsening depression—to cause suicidal thoughts and behaviors. The court therefore finds that Dr. Glass's specific causation opinions are consistent with and supported by Dr. Healy's opinions on general causation.

ii. Differential Diagnosis

Next, Forest argues that Dr. Glass failed to perform a proper differential diagnosis. Forest asserts that Dr. Glass failed to eliminate Mr. Shipley's underlying depression as the cause

of his suicide. Forest also maintains that Dr. Glass's opinions cannot be reliable in light of the fact that Mr. Shipley used Lexapro successfully in 2003.

In his report, Dr. Glass explains that he utilized a "psychological autopsy," which is "a modification of the standard medical 'differential diagnosis' approach." (Glass Report at 5.) This methodology involves a post-mortem risk assessment in which the expert examines the decedent's medical records and the other relevant evidence to "rule in" and then "rule out" various factors that may have contributed to the suicide. For Mr. Shipley, Dr. Glass directly analyzed and discussed his reasons for eliminating certain factors, including Mr. Shipley's underlying depression and previous use of Lexapro.

First, Dr. Glass readily acknowledged that "the major risk factor at the time of [Mr. Shipley's] death was his major depressive disorder." (Id.) But Dr. Glass explained that when Mr. Shipley began taking Lexapro on April 12, 2004, Nurse Christensen had diagnosed Mr. Shipley primarily with "anxiety disorder," mixed with depression. Mr. Shipley was not diagnosed with major depressive disorder until he saw Dr. Julien fifteen days after he began taking Lexapro. According to Dr. Glass, objective facts such as Mr. Shipley's significant weight loss and "horrendous thoughts," justified the updated diagnosis. (Id. at 6.) As Mr. Shipley took Lexapro, his symptoms of depression emerged and increased, which is consistent with Dr. Glass's conclusion that Mr. Shipley experienced worsening depression while using Lexapro. In addition, when asked if Mr. Shipley's condition may have declined simply by virtue of the progression of depression, Dr. Healy responded that, in his experience, untreated depression does not progress as quickly has Mr. Shipley's did. (Hr'g Tr. 49.) After careful review of Dr. Glass's

report and testimony, the court concludes that Dr. Glass considered Mr. Shipley's depression as a possible cause of suicide but ruled it out for objective reasons that were sufficiently explained.

Dr. Glass also accounted for the fact that Mr. Shipley successfully took Lexapro for a few months in 2003. Dr. Glass directly addressed this issue both in his report and at the Daubert hearing. In his report, Dr. Glass described "a well known phenomenon that individuals may become sensitized after an exposure to a medication, and have a different reaction to it when it is given again at a later date." (Glass Report at 7.) Dr. Glass used "sensitized" as a term to describe the "phenomenon that clinicians see all the time," namely, that a patient may have a different reaction to a drug than he or she previously had. (Hr'g Tr. 9-11.) Dr. Glass also recognized that Mr. Shipley's significant financial stressors did not materialize until 2004 and therefore were not present when Mr. Shipley previously took Lexapro:

> [I]t does not appear that in 2003, Mr. Shipley had any particularly acute risk factors for suicide. By contrast, by April 12th of 2004, when Nurse Christensen prescribed Lexapro for a second time, Mr. Shipley was clearly agitated, anxious, and worried about the financial ramifications of his failing business. He had not slept for two nights before that appointment. His risk for suicide at that point in time was significantly higher than it was in 2003, and consequently, anything that added to that risk, including Lexapro, would be extremely dangerous for him.

(Glass Report at 8.)

While Forest may raise its criticisms on cross-examination or through the testimony of its own experts, Dr. Glass's testimony is not rendered inadmissible merely because Mr. Shipley was diagnosed with depression or because he took Lexapro in the past. Dr. Glass utilized a reliable, scientific method to analyze and exclude these potential factors. He was not required to rule out every possible cause of Mr. Shipley's suicide. See Goebel v. Denver & Rio Grande W. R.R. Co., 346 F.3d 987, 998 (10th Cir. 2003) ("[S]everal circuits have held that the failure to rule out *all*

possible alternative causes of an illness does not automatically render an expert's testimony inadmissible."); id. at 999 (affirming district court's conclusion that "failure to exclude explicitly one alternative (depression) did not affect the admissibility of the testimony, although it was an issue the fact finder could consider when assigning weight").

iii. Wellbutrin

Forest maintains that Dr. Glass's opinions should be excluded because he did not attribute Mr. Shipley's suicide to the introduction of Wellbutrin. Dr. Glass responded to this challenge by explaining that he used a differential diagnosis to identify Lexapro as the primary contributing drug. This conclusion was based on the fact that, by the time Mr. Shipley began taking Wellbutrin, his symptoms and depression were already getting much worse. (Hr'g Tr. 29.) In addition, although Wellbutrin has also been associated with suicide, it "has a much lower incidence of people committing suicide than Lexapro has." (Id. 30.) Although Dr. Glass cannot entirely rule out Wellbutrin as a cause of emotional blunting and akathisia, the possible effect of Wellbutrin goes to the weight of Dr. Glass's testimony, not its admissibility.

In sum, Dr. Glass's opinions meet the requirements of Rule 702 and Daubert. Because Dr. Glass is well qualified to testify about specific causation and his opinions are reliable, the court denies Forest's motion to exclude Dr. Glass's testimony.

II. Motions for Summary Judgment

Forest moves for summary judgment on two separate grounds. First, Forest asserts that Mrs. Shipley's claim is barred by federal preemption. Second, Forest maintains that Mrs. Shipley cannot prove the elements of a failure to warn claim.

A. Motion for Summary Judgment Based on Federal Preemption

Under the Supremacy Clause, U.S. Const., Art. VI, cl. 2, state law claims are preempted under certain circumstances, including in cases where the state law "actually conflicts with federal law." English v. Gen. Elec. Co., 496 U.S. 72, 79 (1990). In this category of cases, the Supreme Court has held that state law claims are preempted "where it is impossible for a private party to comply with both state and federal requirements." Id.

As explained by the Seventh Circuit, defendants in prescription drug cases have increasingly raised conflict preemption as a defense:

> [T]he idea of conflict preemption in prescription drug cases is relatively new. Until the early 2000s, prescription drug companies infrequently invoked the preemption defense, and when they did, it rarely succeeded. This changed in 2001 when district courts were inundated with preemption motions in prescription drug cases. In a number of these cases, the FDA filed *amicus* briefs in support of the pharmaceutical industry.[5] In 2006, the FDA also released statements and revised its regulations in an attempt to bolster the drug manufacturers' preemption defense. Not surprisingly, courts began to issue contradicting opinions, which led the Supreme Court to grant certiorari . . . to decide the issue.

Mason v. SmithKline Beecham Corp., 596 F.3d 387, 390-91 (7th Cir. 2010) (citations omitted).

In 2009, the Supreme Court decided Wyeth v. Levine, 555 U.S. 555 (2009), which directly addressed the issue of whether the FDA's labeling requirements preempt liability for

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[5] Similarly here, Forest cites the FDA's amicus brief filed in Kallas v. Pfizer, Inc., Case No. 2:04CV0098 PGC, a case before District Court Judge Paul Cassell in this district. Kallas involved a suicide death in 2002, nearly two years before Mr. Shipley's death. Significantly, the FDA shifted its position related to SSRIs and suicide after it filed its brief in Kallas. While the FDA asserted in Kallas that it would have rejected an attempt to increase the suicide warning on the Pfizer label, soon before Mr. Shipley's death in 2004, the FDA ordered that such a label change be made to the entire class of SSRIs, for both adult and pediatric use. Moreover, the FDA's amicus brief was filed before the Supreme Court's decision in Wyeth v. Levine, 555 U.S. 555 (2009). As discussed below, Wyeth provides the clear evidence standard, which was not in place and not analyzed in any way when the FDA filed its brief in Kallas. For these reasons, the court does not find the FDA's Kallas brief helpful to an analysis of the issues in this case.

failure to warn claims brought under state law. Relying on the FDA's approval of its warning label, Wyeth had argued that "it [was] impossible for it to comply with both the state-law duties . . . and its federal labeling duties." Id. at 568. The Court rejected Wyeth's preemption defense:

> Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application. There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this "changes being effected" (CBE) regulation provides that if a manufacturer is changing a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the product," it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval.

Id. (quoting 21 C.F.R. §§ 314.70(c)(6)(iii)(A), ©).

The Court further concluded that although the FDA has authority to approve or reject label changes, it is not ultimately responsible for drug labels. "[T]he manufacturer bears responsibility for the content of its label at all times" and "is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." Id. at 570-71. When Wyeth learned of the risk involved with its drug, it "had a duty to provide a warning that adequately described that risk, and the CBE regulation permitted it to provide such a warning before receiving the FDA's approval." Id. at 571. With the CBE regulation available, the Court held that preemption does not apply "absent clear evidence that the FDA would not have approved a change to [the drug's] label." Id.

Forest relies on the Supreme Court's later decision in PLIVA, Inc. v. Mensing, 131 S. Ct. 2567 (2011), in which the Court held that preemption applied where a manufacturer of generic prescription drugs had not obtained FDA approval for the changes urged by the plaintiff. Mensing, however, is easily distinguishable because it involved a generic drug. Because labels

for generic drugs must be identical to the labels for corresponding name-brand drugs, manufacturers of generic drugs must apply for and obtain FDA approval before making any label change. The CBE regulation is not an available option to make changes to generic drug labels. The Court in Mensing recognized this distinction and clarified that it was not disturbing the holding in Wyeth. See id. at 2581 ("*Wyeth* is not to the contrary. . . . [T]he federal regulations applicable to Wyeth allowed the company, of its own volition, to strengthen its label in compliance with its state tort duty.").

Because Lexapro is a name-brand drug, Forest had the option to invoke the CBE regulation. So Mensing does not apply; Wyeth controls. And under Wyeth, Forest cannot prevail on its preemption defense absent clear evidence that, before Mr. Shipley's death in 2004, the FDA would have rejected an enhanced suicidality warning in the Lexapro labeling.

I. Newly Acquired Information

Applying Wyeth, Forest contends that it was not possible to use the CBE regulation process because the changes suggested by Mrs. Shipley did not "reflect newly acquired information" as required by the regulation. Forest cites In re Celexa & Lexapro Marketing & Sales Practices Litigation, 779 F.3d 34 (1st Cir. 2015), to support its position. The court agrees with the general rule stated in In re Celexa, namely that "[t]he CBE procedure is only available to make changes that, among other things, are based on 'newly acquired information.'" Id. at 41-42 (quoting 21 C.F.R. § 314.70(c)(6)(iii)). But as the First Circuit recognized, "'newly acquired information' could be an increasing body of data of an inherent risk with the drug." Id. at 42 (citing Wyeth, 555 U.S. at 571). Although the plaintiff in In re Celexa maintained that the Lexapro label should have disclosed that the drug performed approximately the same as a

placebo in a given study, that information was known to the FDA at the time of Lexapro's initial approval. There was no new or increasing body of data that the plaintiff identified. As a result, the court found the state law claims preempted because Forest could not use the CBE regulation to independently change the Lexapro label.

Here, Mrs. Shipley is not requesting a label change that reflects information previously presented during the FDA approval process. Forest contends that the risk of suicide associated with SSRIs has long been a topic of debate and an issue of which the FDA was aware. Responding to a similar argument in Wyeth, the Supreme Court stated,

> As the FDA explained in its notice of the final [CBE regulation] "newly acquired information" is not limited to new data, but also encompasses new analyses of previously submitted data. The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments: If the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for newly acquired information.

555 U.S. at 569 (citations and quotations omitted). Although the record in Wyeth was limited on the issue of newly acquired information, the plaintiff, Ms. Levine, presented evidence of at least twenty cases in which the relevant use of Phenergan led to gangrene and amputation, which is the same injury that Ms. Levine suffered. As a result, the Court concluded, "[A]s amputations continued to occur, Wyeth could have analyzed the accumulating data and added a stronger warning." Id. at 570.

The same is true here. In its March 19, 2004 letter to Forest, the FDA acknowledged that "there ha[d] been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients." (Forest Letter,

Dkt. No. 80-92.) But this general concern became clearer after the FDA received the reanalysis of pediatric data from SSRI sponsors, including Forest. After receiving the full body of requested data, the FDA stated in February 2004 that until that time, the data had not "been provided . . . in a way that would permit [the FDA] to interpret it fully." (Comm. Meeting Tr. 24, Dkt. No. 94-3.) Upon review of the compiled data, the FDA mandated label changes for several SSRIs, including Lexapro. This evidence shows a developing body of data, or "newly acquired information," which would have allowed Forest to use the CBE regulation process.

ii. Clear Evidence

Finally, Forest argues that, even if it could have made a change under the CBE regulation, there is clear evidence that the FDA would not have approved the changes that Mrs. Shipley alleges should have been made. The Supreme Court has not defined what constitutes "clear evidence," but courts have concluded that "the clear evidence standard is a fact based inquiry." Koho v. Forest Laboratories, Inc., 17 F. Supp. 3d 1109, 1118 (W.D. Wash. 2014). While each decision depends on the facts of the particular case, courts applying the clear evidence standard have almost "universally found the manufacturer's evidence inadequate to support conflict preemption." Dobbs v. Wyeth Pharm., 797 F. Supp. 2d 1264, 1270 (W.D. Okl. 2011); see e.g., Mason, 596 F.3d 387; Koho, 17 F. Supp. 3d 1109; Baumgardner v. Wyeth Pharm., 2010 WL 3431671 (E.D. Pa. Aug. 31, 2010); Dorsett v. Sandoz, Inc., 699 F. Supp. 2d 1142 (C.D. Cal. 2010); Aaron v. Wyeth, 2010 WL 653984 (W.D. Pa. Feb. 19, 2010).

The Dobbs decision, on which Forest relies, is the one exception.[6] In Dobbs, the court found clear evidence that the FDA would have rejected the proposed warning because Wyeth actually requested the relevant revisions multiple times, both before and after the decedent's death in 2002. Each time, the FDA rejected Wyeth's proposed changes. The same reasoning does not apply here because Forest never requested a label change that the FDA rejected.

Rather, the court finds the decision in Koho v. Forest Laboratories, Inc., 17 F. Supp. 3d 1109 (W.D. Wash. 2014), applicable to the facts of this case. In Koho, the court rejected Forest's preemption defense because Forest did not propose any modifications to Celexa's label before the plaintiff's death in 2002. "In light of this evidence, defendants' speculation regarding how the FDA would have viewed such a warning does not constitute clear evidence that the FDA would have rejected the particular warning at issue in this case." Id. at 1119.

Here, Forest has not produced any evidence to show that it attempted to change the Lexapro label. Forest never applied for advanced FDA approval for an increased suicidality warning and never utilized the CBE regulation for that purpose.

Forest nonetheless maintains that there is clear evidence that the FDA would not have allowed Forest to edit the Lexapro label before Mr. Shipley died on April 29, 2004. First, Forest correctly states that FDA regulations prevented it from implementing a "black box" warning or distributing a "Medication Guide." See 21 C.F.R. § 201.80(e); 21 C.F.R. § 208.24(a). But Mrs. Shipley has abandoned any argument that Forest could have added a black box warning or Medication Guide. She instead "assert[s] that Forest could have used the CBE Regulation to add

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[6] The Dobbs court in fact "explicitly recognized that its decision diverged from that of every other court that had addressed the issue." Muzichuck v. Forest Labs., Inc., Civil Action No. 1:07CV16, 2015 WL 235226, at *8 (N.D.W.V. Jan. 16, 2015).

language in the warnings section that was substantially similar to the language FDA itself began to require the month following Kurt Shipley's death, and still requires to this day." (Pl.'s Resp. and Mem. in Opp'n to Forest's Mot. for Summ. J. Based on Preemption at 5, Dkt. No. 94.)

Forest responds by relying on the opinions of its expert witness, Dr. Thomas Laughren, who asserts that the FDA would not have approved the changes proposed by Mrs. Shipley. Although Dr. Laughren previously worked for the FDA, he confirmed that he no longer works for the FDA and his opinions do not reflect the FDA's official position. (Laughren Dep. at 209, Dkt. No. 95-1.) Dr. Laughren is not authorized to bind or speak on behalf of FDA in any way and has not attempted to do so. (Id.) His testimony merely reflects his own opinion about how the FDA may have viewed an updated label if Forest had proposed one before Mr. Shipley's death. By itself, Dr. Laughren's opinion does not satisfy the clear evidence standard.

Moreover, Dr. Laughren's testimony is countered by evidence related to the FDA's actual conduct in the months before Mr. Shipley's death. About a month before Mr. Shipley's death, the FDA sent its letter dated March 19, 2004. Rather than retaining the existing warning, which merely stated that suicide attempts may be an inherent risk of depression, the FDA directed Forest to enhance the Lexapro label to warn that Lexapro may induce suicide. The FDA also required updates to instruct health care providers to closely monitor patients for suicidal thoughts and behaviors, especially at the beginning of treatment. This is precisely the type of warning that Mrs. Shipley alleges should have been in place before her husband was prescribed Lexapro. Viewing this record in the light most favorable to Mrs. Shipley, there is not clear evidence that the FDA would have rejected a heightened warning concerning the correlation between suicidality and SSRIs, particularly in light of the fact that, before Mr. Shipley began taking

Lexapro in April 2004, the FDA specifically asked Forest to make such a change. As a result, preemption does not apply to bar Mrs. Shipley's claim.

B. Motion for Summary Judgment

In its second motion for summary judgment, Forest asserts that it did not owe a duty to warn about the potential adverse effects of Lexapro. To the extent it did owe a duty, Forest maintains that it fulfilled its duty by providing warnings to Mr. Shipley's healthcare providers. In addition, Forest argues that Mrs. Shipley cannot prove the causation element of her failure to warn claim.

I. Forest's Liability as a Non-Manufacturer

Forest first argues that Mrs. Shipley has sued the wrong entity because it does not manufacture or distribute Lexapro and therefore cannot be liable under Utah products liability law. The court acknowledges that a separate entity, Forest Laboratories Ireland Limited, manufactures Lexapro. But the manufacturer is not the only entity who may be liable for failure to warn about a drug's risks. Even though a different entity actually manufactures the drug, Forest is the FDA sponsor for Lexapro. And "[w]arnings for Lexapro are drafted by the regulatory affairs department of Forest Laboratories, Inc." (Weinberger Decl. ¶ 6, Dkt. No. 80-66.) Moreover, FDA letters about label changes were not addressed to Lexapro's manufacturer; the letters were addressed to Forest. (See 03/19/04 FDA Letter, Dkt. No. 80-92.) In short, Forest facilitates FDA approval and is responsible for the Lexapro label.

At oral argument, Forest conceded that it "is a link in the chain, but in the sense that you have to have FDA approval in order to have the product go to market." (Hr'g Tr. 104.) Although Forest argues that the chain of distribution is separate and independent from its role related to

Lexapro, the court does not find this argument persuasive. Without Forest, Lexapro would not be sold as an FDA-approved drug. In other words, Forest an indispensable player in the chain of distribution for Lexapro. Under Utah law, Forest's role is more than sufficient to hold it liable for failure to warn. See Jackson v. Philip Morris Inc., 46 F. Supp. 2d 1217, 1229 (D. Utah 1998) ("[U]nder Utah strict products liability law, a plaintiff may sue the distributor of an unreasonably dangerous product so long as the distributor is sufficiently placed within the chain of distribution of the product from the manufacturer to the ultimate consumer.").

ii. Duty and Proximate Cause

The court's analysis of duty and proximate cause requires consideration of two interrelated principles of Utah law. First, Utah courts recognize the learned intermediary rule, that "manufacturers of prescription drugs have a duty to warn only the physician prescribing the drug, not the end user or patient." Schaerrer v. Stewart's Plaza Pharmacy, Inc., 2003 UT 43, ¶ 20, 79 P.3d 922. "A manufacturer will be held directly liable to the patient for breach of the duty to make timely and adequate warnings to the medical profession of any dangerous side effects produced by its drug of which it knows or has reason to know." Id. Second, "under Utah law, there is a presumption that warnings will be heeded." Dowdy v. Coleman Co., No. 1:11CV45DAK, 2012 WL 4024451, at *5 (D. Utah Sept. 12, 2012). In other words, "in cases in which it cannot be demonstrated what the plaintiff would have done had he or she been adequately warned, the plaintiff should be afforded a rebuttable presumption that he or she would have followed an adequate warning had one been provided." House, 886 P.2d at 553. Other courts applying the heeding presumption in prescription drug cases have further held that if the defendant presents evidence to rebut the presumption, "the plaintiff must produce sufficient

evidence to create a triable issue on the question of causation." Garside v. Osco Drug, Inc., 976 F.2d 77, 81 (1st Cir. 1992) (applying Massachusetts law).

Forest argues that, under the learned intermediary rule, it did not have a duty to warn Mr. Shipley about the potential adverse effects of Lexapro because its sole duty was to warn health care professionals. According to Forest, it indisputably fulfilled its duty because Mr. Shipley's treating providers, Dr. Julien and Nurse Christensen, both testified that they knew at the time they prescribed Lexapro that it and other SSRIs could contribute to suicidality. Relying on the providers' testimony, Forest also concludes that it has rebutted the heeding presumption because additional warnings would not have changed the outcome for Mr. Shipley.

Although Forest is correct that its duty was limited to warning health care providers, the evidence does not establish as a matter of law that Mr. Shipley's providers had the necessary warning information when prescribing Lexapro to Mr. Shipley. Nurse Christensen initially testified that he was aware of the debate about the possible link between SSRIs and suicidality, and he understood that SSRIs could potentially worsen symptoms of depression or anxiety rather than lessening them. (Christensen Dep. at 26-27, Dkt. No. 78-45.) But Nurse Christensen later clarified that he does not know when he first learned about the relationship between suicide and SSRIs, and he could not definitively answer whether he was aware of the debate in 2004. (Id. at 31.) Dr. Julien similarly testified that although he was generally aware of the debate related to SSRIs and suicidality, he would expect Forest to inform providers if it knew that Lexapro could cause or contribute to the development of suicidality. (Julien Dep. at 19, 28-29, 68, Dkt. No. 78-48.) Dr. Julien confirmed that when he prescribed Lexapro to Mr. Shipley in April 2004, the label did not contain the bolded language that was later added: "Nevertheless, patients being

treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose change, either increases or decreases." (Id. at 84.) This added information would affect Dr. Julien's prescribing habits and the way he counsels his patients. (Id. at 68.)

When Mr. Shipley began taking Lexapro for the second time on April 12, 2004, the drug's label merely warned about the need to monitor high-risk patients and the general correlation between depression and suicide. It did not warn that Lexapro could increase or induce suicidal thoughts and behavior. And it did not instruct providers to inform patients and their families about the specific risk of suicide associated with SSRIs. Although Nurse Christensen and Dr. Julien may have been generally aware of the need to monitor patients for suicidal behavior, general awareness is not the same as receiving a specific warning to closely observe patients for suicidality when taking a specific drug. Viewing the evidence in the light most favorable to Mrs. Shipley, the court cannot conclude as a matter of law that Forest fulfilled its duty to provide an adequate warning to Mr. Shipley's health care providers.

Moreover, even assuming that Nurse Christensen and Dr. Julien knew that patients taking Lexapro should be observed for signs of suicidality, the heeding presumption is still subject to dispute. Forest maintains that it has rebutted the presumption and Mrs. Shipley cannot prove proximate cause because Nurse Christensen and Dr. Julien testified that even with the current enhanced warnings, they continue to prescribe Lexapro. Forest bases its position on the premise that Mrs. Shipley must prove that Lexapro would not have been prescribed if additional warnings had been given. But that is not the applicable burden or the claim that Mrs. Shipley asserts.

Mrs. Shipley claims that if a better warning had been in place when her husband took Lexapro, his medical providers would have monitored him more closely and would have warned her to do the same, especially in the early days of treatment, which is when Mr. Shipley committed suicide. Mrs. Shipley maintains that, if she had been given such a warning, she would have watched her husband for signs of suicidality.

In addition, both Dr. Julien and Nurse Christensen testified that they now counsel patients more emphatically about the possible onset of suicidal behavior when taking SSRIs. Nurse Christensen testified that he would have reviewed FDA Public Health Advisories such as the one issued on March 22, 2004. And he believes he provided warnings similar to the warnings later added to the Lexapro labeling. But again, Nurse Christensen clarified that he would have warned about the emergence of suicidal thinking if it was part of the information and knowledge that he had. After reading the updated labeling at his deposition, Nurse Christensen testified that he believed he would have given Mr. Shipley a similar warning, but if he had the exact warning that was later added to the Lexapro label, his patient counseling "would have been more succinct." (Christensen Dep. at 75-76.) Dr. Julien also testified that he pays attention to warning labels, and with the updated Lexapro label, he provides additional counseling to his patients and their families to watch for suicide warning signs.

The court will afford Mrs. Shipley the benefit of the heeding presumption and will presume that Nurse Christensen and Dr. Julien would have provided additional warnings to Mr. and Mrs. Shipley if such warnings had been included the Lexapro labeling. As outlined above, both providers testified that label changes affect their practice and their patient counseling has in fact changed with the updated Lexapro label. Although Forest cites evidence to the contrary, this

merely confirms that there is a disputed issue of fact for the jury to resolve. The jury should decide whether a different warning label would have affected the guidance given by Mr. Shipley's providers and whether an increased warning would have allowed better monitoring that may have prevented Mr. Shipley's suicide.

Finally, in response to the argument that Forest improperly delayed its implementation of the FDA's required updates, Forest maintains that its actions were indisputably reasonable. While a jury could agree that Forest acted as quickly as possible, a jury could also conclude that Forest should have alerted healthcare providers of the Lexapro label changes before it did. Forest knew as early as March 19, 2004, that the FDA was requiring label changes to make clear that Lexapro could be related to increased or emerging suicidality. Mrs. Shipley argues that, at this point, Forest should have done more to inform providers about the upcoming changes. For example, Forest could have issued "Dear Doctor" letters. Forest also could have instructed its sales representatives to alert providers about the new, heightened warnings. Indeed, Lexapro sales representatives visited Nurse Christensen's and Dr. Julien's offices multiple times between the date of the FDA's March 19, 2004 letter and the date of Mr. Shipley's death. Rather than telling providers that a label change was coming soon, sales representatives were told that they should not proactively discuss the new labeling.

Moreover, after the FDA told Forest on April 19, 2004, to immediately change the Lexapro label using the CBE regulation process, Forest did not follow this instruction. Rather than utilize the CBE regulation—which would have allowed immediate, unilateral change to the Lexapro label while waiting for FDA approval—Forest submitted its updated label to the FDA

for advanced approval. Forest indicated that it planned to implement the updated label by May 31, 2004, and the FDA approved the changes on May 20, 2004.

With this evidence, Mrs. Shipley maintains that Forest did not timely update its warnings when it could have and did not take other independent steps to alert providers that the warnings would be significantly changed. The jury should have the opportunity to consider this evidence and determine whether Forest's efforts to provide warnings were reasonable.

ORDER

For the foregoing reasons, the court enters the following order:

1. Defendant Forest Laboratories, Inc.'s Motion to Exclude the Testimony of George S. Glass, M.D. (Dkt. No. 78) is DENIED.

2. Forest Laboratories, Inc.'s Motion for Summary Judgment Based on Federal Preemption (Dkt. No. 79) is DENIED.

3. Forest Laboratories, Inc.'s Motion for Summary Judgment (Dkt. No. 80) is GRANTED IN PART AND DENIED IN PART. Because Mrs. Shipley concedes that summary judgment should be granted on her design defect and manufacturing defect claims, the court grants summary judgment on these claims. Forest's motion is denied to the extent it seeks summary judgment on Mrs. Shipley's failure to warn claim.

DATED this 13th day of July, 2015.

BY THE COURT:

Tena Campbell

TENA CAMPBELL
U.S. District Court Judge